

Form PTO-1449 INFORMATION DISCLOSURE CITATION IN AN APPLICATION (Use several sheets if necessary) DEC 03 2001			Docket Number (Optional) CIBT-P01-080	Application Number 09/724,964
			Applicant Tessa Crompton	
			Filing Date November 28, 2000	Group Art Unit 1632 1646

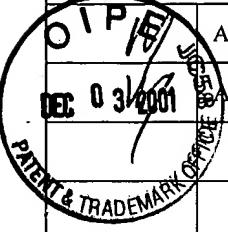
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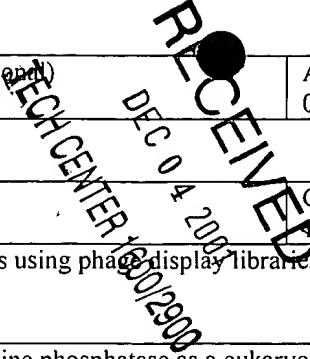
## U.S. PATENT DOCUMENTS

EXAMINER PATENT TRADEMARK OFFICE	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
				CLASS		
WJ	AA 5,328,470	7/12/94	Nabel et al.			
	AB 5,286,654	2/15/94	Cox et al.			
	AC 5,266,488	11/30/93	Ordahl et al.			
	AD 5,264,564	11/23/93	Matteucci			
	AE 5,256,775	10/26/93	Froehler			
	AF 5,223,409	6/29/93	Ladner et al.			
	AG 5,223,408	6/29/93	Goeddel et al.			
	AH 5,198,346	3/30/93	Ladner et al.			
	AI 5,176,996	1/5/93	Hogan et al.			
	AJ 5,096,815	3/17/92	Ladner et al.			
	AK 4,980,286	12/25/90	Morgan et al.			
WJ	AL 4,868,116	9/19/89	Morgan et al.			

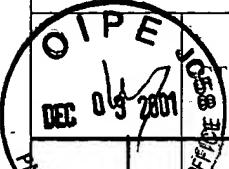
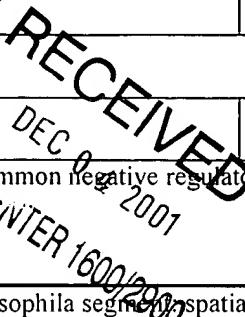
## FOREIGN PATENT DOCUMENTS

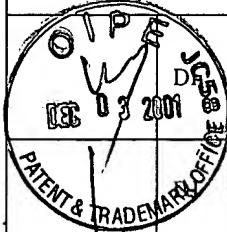
	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	Translation	
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WJ	AM WO 96/29411	9/26/96	PCT			
	AN WO 96/17924	6/13/96	PCT			
	A0 WO 95/31560	11/23/95	PCT			
	AP WO 95/18856	7/13/95	PCT			
	AQ WO 93/25234	12/23/93	PCT			
	AR WO 93/09222	5/13/93	PCT			
	AS WO 92/15679	9/17/92	PCT			
	AT WO 92/09690	6/11/92	PCT			
	AU WO 92/07573	5/14/92	PCT			
	AV WO 90/02809	3/22/90	PCT			
	AW WO 89/07136	8/10/89	PCT			
WJ	AX WO 89/05345	6/15/89	PCT			

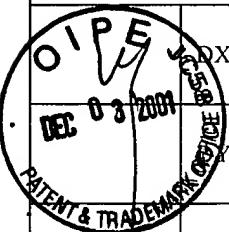
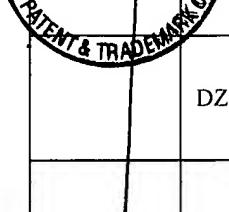
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 <b>DEC 03 2001</b>		AY	WO 89/02468	3/23/89	PCT
		AZ	WO 88/06630	9/7/88	PCT
<b>OTHER DOCUMENTS</b> <i>(Including Author, Title, Date, Pertinent Pages Etc.)</i>					
	BA	Arkin and Yourvan, 1992, "An algorithm for protein engineering: simulations of recursive ensemble mutagenesis", Proc. Natl. Acad. Sci. USA 89:7811-7815.			
	BB	Armentano et al., 1990, "Expression of human factor IX in rabbit hepatocytes by retrovirus-mediated gene transfer: potential for gene therapy of hemophilia B", Proc. Natl. Acad. Sci. USA 87:6141-6145.			
	BC	Baldwin et al., 1984, "Cloning of the luciferase structural genes from Vibrio harveyi and expression of bioluminescence in Escherichia coli", Biochemistry 23:3663-3667			
	BD	Barbas et al., 1992, "Semisynthetic combinatorial antibody libraries: a chemical solution to the diversity problem", Proc. Natl. Acad. Sci. USA 89:4457-4461			
	BE	Bass et al., 1990, "Hormone phage: an enrichment method for variant proteins with altered binding properties", Proteins 8:309-314			
	BF	Bear et al., 1992, "Purification and functional reconstitution of the cystic fibrosis transmembrane conductance regulator (CFTR)", Cell 68:809-818			
	BG	Ben-Bassat et al., 1987, "Processing of the initiation methionine from proteins; properties of the Escherichia coli methionine aminopeptidase and its gene structure", J. Bacteriol. 169:751-757			
	BH	Benoist et al., 1981, "In vivo sequence requirements of the SV40 early promotor region", Nature 290:304-310			
	BI	Berkner et al., 1988, "Development of adenovirus vectors for the expression of heterologous genes", Biotechniques 6:616-629			
	BJ	Borle, 1990, "An overview of techniques for the measurement of calcium distribution, calcium fluxes, and cytosolic free calcium in mammalian cells", Environ. Health Perspect. 84:45-56			
	BK	Bumcrot et al., 1995, "Proteolytic processing yields two secreted forms of sonic hedgehog", Mol. Cell. Biol. 15:2294-2303			
	BL	Chang et al., 1994, "Products, genetic linkage and limb patterning activity of a murine hedgehog gene", Development 120:3339-3353			
	BM	Chen et al., "Gene therapy for brain tumors: regression of experimental gliomas by adenovirus-mediated gene transfer in vivo", Proc. Natl. Acad. Sci. USA 91:3054-3057			
	BN	Chowdhury et al. 1991, "Long-term improvement of hypercholesterolemia after ex vivo gene therapy in LDLR-deficient rabbits", Science 254:1802-1805			

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		Clackson et al., 1991, "Making antibody fragments using phage display libraries", Nature 352:624-628	
		Cullen and Malim, 1992, "Secreted placental alkaline phosphatase as a eukaryotic reporter gene", Methods Enzymol. 216:362-368	
		BQ	Cwirla et al., 1990, "Peptides on phage: a vast library of peptides for identifying ligands", Proc. Natl. Acad. Sci. USA 87:6378-6382.
		BR	Dai et al., 1992, "Gene therapy via primary myoblasts: long-term expression of factor IX protein following transplantation in vivo", Proc. Natl. Acad. Sci. USA 89:10892-10895
		BS	Dann et al., 1986, "Human renin: a new class of inhibitors", Biochem. Biophys. Res. Commun. 134:71-77
		BT	Danos and Mulligan, 1988, "Safe and efficient generation of recombinant retroviruses with amphotropic and ecotropic host ranges", Proc. Natl. Acad. Sci. USA 85:6460-6464
		BU	Delagrange et al., 1993, "Recursive ensemble mutagenesis", Protein Eng. 6:327-331
		BV	Dev et al., 1994, "Electrochemotherapy--a novel method of cancer treatment", Cancer Treat. Rev. 20:105-115
		BW	Devlin et al., 1990, "Random peptide libraries: a source of specific protein binding molecules", Science 249:404-406
		BX	DeWet et al., 1987, "Firefly luciferase gene: structure and expression in mammalian cells", Mol. Cell Biol. 7:725-737
		BY	Eglitis et al., 1985, "Gene expression in mice after high efficiency retroviral-mediated gene transfer", Science 230:1395-1398
		BZ	Ekker et al., 1995, "Patterning activities of vertebrate hedgehog proteins in the developing eye and brain", Curr. Biol. 5:944-955
		CA	Ellison et al., 1991, "Epitope-tagged ubiquitin. A new probe for analyzing ubiquitin function", J. Biol. Chem. 266:21150-21157
		CB	Ellman et al., 1958, "A colorimetric method for determining low concentrations of mercaptans", Arch. Biochem. Biophys. 74:443
		CC	Engebrecht and Silverman, 1984, "Identification of genes and gene products necessary for bacterial bioluminescence", Proc. Natl. Acad. Sci. USA 81:4154-4158
		CD	Ettienne-Julian et al., 1992, "The efficiency of cell targeting by recombinant retroviruses depends on the nature of the receptor and the composition of the artificial cell-virus linker", J. Gen. Virol. 73 ( Pt 12):3251-3255

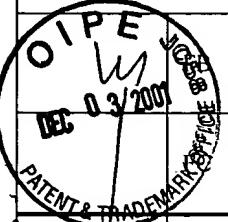
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 		Ewenson et al., 1986, "Ketomethylene pseudopeptide analogues of substance P: synthesis and biological activity", J. Med. Chem. 29:295-299	
		CF	Ferry et al., 1991, "Retroviral-mediated gene transfer into hepatocytes in vivo", Proc. Natl. Acad. Sci. USA 88:8377-8381
		CG	Fuchs et al., 1991, "Targeting recombinant antibodies to the surface of <i>Escherichia coli</i> : fusion to a petidoglycan associated lipoprotein", Bio/Technology 9:1370-1371
		CH	Gallop et al., 1994, "Applications of combinatorial technologies to drug discovery. 1. Background and peptide combinatorial libraries", J. Med. Chem. 37:1233-1251
		CI	Gordon et al., 1985, "Design of peptide derived amino alcohols as transition-state analog inhibitors of angiotensin converting enzyme", Biochem. Biophys. Res. Commun. 126:419-426
		CJ	Goud et al., 1983, "Antibody-mediated binding of a murine ecotropic Moloney retroviral vector to human cells allows internalization but not the establishment of the proviral state", Virology 163:251-254
		CK	Goward et al, 1992, "Molecular evolution of bacterial cell-surface proteins", Trends Biochem. Sci. 18:136-140 Review.
		CL	Graham et al., 1991, "Manipulation of adenovirus vectors" <i>Methods in Molecular Biology</i> (Humana, Clifton, NJ) Vol. 7 pp. 109-127
		CM	Griffiths et al., 1993, "Human anti-self antibodies with high specificity from phage display libraries", EMBO J. 12:725-734
		CN	Gunning et al., 1997, "A human beta-actin expression vector system directs high-level accumulation of antisense transcripts", Proc. Natl. Acad. Sci. USA 84:4831-4835
		CO	Gustin et al., 1993, "Characterization of the role of individual protein binding motifs within the hepatitis B virus enhancer I on X promoter activity using linker scanning mutagenesis", Virology 193:653-660
		CP	Habig et al., 1974, "Glutathione S-transferases. The first enzymatic step in mercapturic acid formation", J. Biol. Chem. 249:7130-7139
		CQ	Hahn et al., 1996, "Mutations of the human homolog of <i>Drosophila</i> patched in the nevoid basal cell carcinoma syndrome", Cell 85:841-851
		CR	Haj-Ahmad et al., 1986, "Development of a helper-independent human adenovirus vector and its use in the transfer of the herpes simplex virus thymidine kinase gene", J. Virol. 57:267-274
		CS	Hall et al., 1983, "Expression and regulation of <i>Escherichia coli</i> lacZ gene fusions in mammalian cells", J. Mol. Appl. Genet. 2:101-109

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 		Hammerschmidt et al., 1996, "Protein kinase A is a common negative regulator of Hedgehog signaling in the vertebrate embryo", Genes Dev. 10:647-658	
		 Hidalgo and Ingham, 1990, "Cell patterning in the Drosophila segment: spatial regulation of the segment polarity gene patched", Development 110:291-301	
		CV	Hochuli et al., 1987, "New metal chelate adsorbent selective for proteins and peptides containing neighbouring histidine residues", J. Chromatogr. 411:177-184
		CW	Huber et al., 1991, "Retroviral-mediated gene therapy for the treatment of hepatocellular carcinoma: an innovative approach for cancer therapy", Proc. Natl. Acad. Sci. USA 88:8039-8043
		CX	Hui et al., 1994, "Expression of three mouse homologs of the Drosophila segment polarity gene <i>cubitus interruptus</i> , <i>Gli</i> , <i>Gli-2</i> , and <i>Gli-3</i> , in ectoderm- and mesoderm-derived tissues suggests multiple roles during postimplantation development", Dev. Biol. 162:402-413
		CY	Huston et al., 1988, "Protein engineering of antibody binding sites: recovery of specific activity in an anti-digoxin single-chain Fv analogue produced in <i>Escherichia coli</i> ", Proc. Natl. Acad. Sci. USA 85:5879-5883
		CZ	Hwu et al., 1993, "Functional and molecular characterization of tumor-infiltrating lymphocytes transduced with tumor necrosis factor-alpha cDNA for the gene therapy of cancer in humans", J. Immunol. 150:4104-4115
		DA	Hynes, 1987, "Integrins: a family of cell surface receptors", Cell 48:549-554
		DB	Hynes, 1992, "Integrins: versatility, modulation, and signaling in cell adhesion", Cell 69:11-25
		DC	Ike et al., 1983, "Solid phase synthesis of polynucleotides. VIII. Synthesis of mixed oligodeoxyribonucleotides by the phosphotriester solid phase method", Nucleic Acids Res. 11:477-488
		DD	Itakura et al., 1981, Recombinant DNA, Proc. 3 <sup>rd</sup> Cleveland Symposium On Macromolecules, A.G. Walton, ed. (Elsevier, Amsterdam) pp. 273-289
		DE	Itakura et al., 1984, "Expression in <i>Escherichia coli</i> of a chemically synthesized gene for the hormone somatostatin", Science 198:1056-1063
		DF	Itakura et al., 1984, "Synthesis and use of synthetic oligonucleotides", Annu. Rev. Biochem. 53:323-356
		DG	Johnson et al., 1996, "Human homolog of patched, a candidate gene for the basal cell nevus syndrome", Science 272:1668-1671
		DH	Jones et al., 1979, "Isolation of adenovirus type 5 host range deletion mutants defective for transformation of rat embryo cells", Cell 17:683-689

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				Karasuyama et al., 1989, "Autocrine growth and tumorigenicity of interleukin 2-dependent helper T cells transfected with IL-2 gene", <i>J. Exp. Med.</i> 169:1025-1032
	DK	Kay et al., 1992, "Hepatic gene therapy: persistent expression of human alpha 1-antitrypsin in mice after direct gene delivery in vivo", <i>Hum. Gene Ther.</i> 3:641-647		
	DL	Kinzler et al., 1990, "The GLI gene encodes a nuclear protein which binds specific sequences in the human genome", <i>Mol. Cell. Biol.</i> 10:634-642		
	DM	Klessig et al., 1984, "Introduction, stable integration, and controlled expression of a chimeric adenovirus gene whose product is toxic to the recipient human cell", <i>Mol. Cell. Biol.</i> 4:1354-1362		
	DN	Kornblihtt et al., 1985, "Primary structure of human fibronectin: differential splicing may generate at least 10 polypeptides from a single gene", <i>EMBO J.</i> 4:1755-1759		
	DO	Kube et al., 1995, "Isolation of the human interleukin 10 promoter. Characterization of the promoter activity in Burkitt's lymphoma cell lines", <i>Cytokine</i> 7:1-7		
	DP	Lai et al., 1995, "Patterning of the neural ectoderm of <i>Xenopus laevis</i> by the amino-terminal product of hedgehog autoprotolytic cleavage", <i>Development</i> 121:2349-2360		
	DQ	Lee et al., 1992, "Secretion and localized transcription suggest a role in positional signaling for products of the segmentation gene hedgehog", <i>Cell</i> 71:33-50		
	DR	Lee et al., 1994, "Autoproteolysis in hedgehog protein biogenesis", <i>Science</i> 266:1528-1537		
	DS	Lyons and Nelson, 1984, "An immunological method for detecting gene expression in yeast colonies", <i>Proc. Natl. Acad. Sci. USA</i> 81:7426-7430		
	DT	Marigo and Tabin, 1996, "Regulation of patched by sonic hedgehog in the developing neural tube", <i>Proc. Natl. Acad. Sci. USA</i> 93:9346-9351		
	DU	Marigo et al., 1996, "Conservation in hedgehog signaling: induction of a chicken patched homolog by Sonic hedgehog in the developing limb", <i>Development</i> 122:1225-1233		
	DV	Marks et al., 1992, "Molecular evolution of proteins on filamentous phage. Mimicking the strategy of the immune system", <i>J. Biol. Chem.</i> 267:16007-16010		
✓	DW	Marti et al., 1995, "Distribution of Sonic hedgehog peptides in the developing chick and mouse embryo", <i>Development</i> 121:2537-2547		
		Miller et al., 1987, "N-terminal methionine-specific peptidase in <i>Salmonella typhimurium</i> ", <i>Proc. Natl. Acad. Sci. USA</i> 84:2718-2722		

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 		Miller, 1990, "Progress toward human gene therapy", Blood 76:2572-600/2900	
	DX	Narang, 1983, "DNA synthesis", Tetrahedron 39:3-22	
	DZ	Neda et al., 1991, "Chemical modification of an ecotropic murine leukemia virus results in redirection of its target cell specificity", J. Biol. Chem. 266:14143-14146	
	EA	Newton et al., 1983, "Transfer of band 3, the erythrocyte anion transporter, between phospholipid vesicles and cells", Biochemistry 22:6110-6117	
	EB	Orenic et al., 1996, "Cloning and characterization of the segment polarity gene <i>cubitus interruptus Dominant of Drosophila</i> ", Genes Dev. 4:1053-1067	
	EC	Partis et al., 1983, "Cross-linking of protein by $\omega$ -maleimido alkanoyl n-hydroxysuccinimido esters", J. Pro. Chem. 2:263	
	ED	Pepinsky et al., 1998, "Identification of a palmitic acid-modified form of human Sonic hedgehog", J. Biol. Chem. 273:14037-14045	
	EE	Pierschbacher et al., 1984, "Cell attachment activity of fibronectin can be duplicated by small synthetic fragments of the molecule", Nature 309:30-33	
	EF	Pierschbacher et al., 1987, "Influence of stereochemistry of the sequence Arg-Gly-Asp-Xaa on binding specificity in cell adhesion", J. Biol. Chem. 262:17294-17298	
	EG	Porter et al., 1995, "The product of hedgehog autoproteolytic cleavage active in local and long-range signalling", Nature 374:363-366	
	EH	Porter et al., 1996, "Hedgehog patterning activity: role of a lipophilic modification mediated by the carboxy-terminal autoprocessing domain", Cell 86:21-34	
	EI	Preat et al., 1990, "A putative serine/threonine protein kinase encoded by the segment-polarity fused gene of <i>Drosophila</i> ", Nature 347:87-89	
	EJ	Reber et al., 1987, "Hydrophobic properties of the beta 1 and beta 2 subunits of the rat brain sodium channel", J. Biol. Chem. 262:11369-11374	
	EK	Riddles et al., 1979, "Ellman's reagent: 5,5'-dithiobis(2-nitrobenzoic acid)--a reexamination", Anal. Biochem. 94:75-81	
	EL	Roberts et al., 1992, "Directed evolution of a protein: selection of potent neutrophil elastase inhibitors displayed on M13 fusion phage", Proc. Natl. Acad. Sci. USA 89:2429-2433	
	EM	Roelink et al., 1995, "Floor plate and motor neuron induction by different concentrations of the amino-terminal cleavage product of sonic hedgehog autoproteolysis", Cell 81:445-455	

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	EP	Rosenfeld et al., 1992, "In vivo transfer of the human cystic fibrosis transmembrane conductance regulator gene to the airway epithelium", Cell 68:143-155	
	EQ	Roux et al., 1989, "A versatile and potentially general approach to the targeting of specific cell types by retroviruses: application to the infection of human cells by means of major histocompatibility complex class I and class II antigens by mouse ecotropic murine leukemia virus-derived viruses", Proc. Natl. Acad. Sci. USA ;86:9079-9083	
	ER	Ruosahti et al., 1987, "New perspectives in cell adhesion: RGD and integrins", Science 238:491-497	
	ES	Sato et al., 1986, "Synthesis and antibiotic activity of a gramicidin s analogue containing bicyclic beta-turn dipeptides", J. Chem. Soc. Perkin Trans. 1:1231	
	ET	Sato et al., 1995, "Structure and regulation of the gene encoding the neuron-specific protein kinase C substrate neurogranin (RC3 protein)", J. Biol. Chem. 270:10314-10322	
	EU	Scott et al., 1990, "Searching for peptide ligands with an epitope library", Science 249:386-390	
	EV	Sprague et al., 1983, "Expression of a recombinant DNA gene coding for the vesicular stomatitis virus nucleocapsid protein", J. Virol. 45:773-781	
	EW	Stein et al., 1988, "Oligodeoxynucleotides as inhibitors of gene expression: a review", Cancer Res. 48:2659-2668 Review.	
	EX	Tabata et al., 1992, "The Drosophila hedgehog gene is expressed specifically in posterior compartment cells and is a target of engrailed regulation", Genes Dev. 6:2635-2645	
	EY	Templeton et al., 1984, "N-terminal amino acid sequences of the polyoma middle-size T antigen are important for protein kinase activity and cell transformation", Mol. Cell. Biol. 4:817-821	
	EZ	Therond et al., 1993, "Molecular organisation and expression pattern of the segment polarity gene fused of Drosophila melanogaster", Mech. Dev. 44:65-80	
↓	FA	Toh et al., 1989, "Isolation and characterization of a rat liver alkaline phosphatase gene. A single gene with two promoters", Eur. J. Biochem. 182:231-237	

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	FD	Wen et al., 1995, "The expression and intracellular distribution of the heat-stable protein kinase inhibitor is cell cycle regulated", J. Biol. Chem. 270:2041-2046.	
	FE	Wilson et al., 1988, "Retrovirus-mediated transduction of adult hepatocytes", Proc. Natl. Acad. Sci. USA 85:3014-3018	
	FF	Wolfe et al., 1992, "Herpesvirus vector gene transfer and expression of beta-glucuronidase in the central nervous system of MPS VII mice", Nat. Genet. 1:379-384	
	FG	Yamada et al., 1985, "Overproduction of the protein product of a nonselected foreign gene carried by an adenovirus vector", Proc. Natl. Acad. Sci. USA 82:3567-3571	
	FH	Yamamoto et al., 1980, "Identification of a functional promoter in the long terminal repeat of Rous sarcoma virus", Cell 22:787-797	
	FI	Youvan et al., 1992, <u>Parallel Problem Solving from Nature</u> (Elsevier Publishing Co., Amsterdam) pp. 401-410	
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